REMARKS

Claims 48-75 are active in this application.

Support for the expression construct in, e.g., Claim 48 is found in Figure 9D and Example 3 on page 64. The inducible promoter is described, for example, on pages 14-16 and l page 33-34 (Table 2). The method claims, e.g., Claim 56, are described on page 35 *et seq* and exemplified in Example 3, which starts on page 64. The composition claims, Claims 68-75, find support on page 54-56. No new matter is added by these amendments.

Applicants wish to thank Examiner Priebe for the interview granted to the Applicants' undersigned representative on January 13, 2003. During this interview, three main issues were discussed: (1) the new matter objection concerning the change values in Table 4; (2) the enablement rejection concerning *in vivo* expression; and (3) the prior art rejections, generally, with particular emphasis on the Bromley et al disclosure (EP 0299127). Each is addressed in turn below.

THE REJECTION UNDER 35 U.S.C.§ 132

During the interview, the Applicants' undersigned representative pointed out that the changes to Table 4 were due to inadvertent errors when the actual data were reproduced into tabular form. Specifically, the Applicants' undersigned representative pointed to the original figure from which these data were derived and noted the points of error. The Examiner suggested that a Declaration from one of the named inventors outlining why the error occurred would be helpful to address the rejection under 35 U.S.C. § 132. Accordingly, Applicants provide herewith a declaration from Dr. Eugene Gerner, one of the named inventors, who refers to and points out the errors which occurred. Dr. Gerner also points out that the errors occurred without any deceptive intent.

In light of this Declaration, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 132.

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

the claims as presented herein are directed to an expression construct and a method of expressing a selected polynucleotide in a cell by providing an expression construct. As the method may relate to *in vivo* expression, the Examiner suggested that the Applicants point out to *in vivo* uses for gene transfer with the expression construct other than therapeutic *in vivo* uses. These uses are outlined below.

On page 3, last paragraph, and page 14, first paragraph, the Applicants have described that the vectors can be used to assess transgene expression in a cell.

On page 25, last paragraph, the Applicants have described that the expression construct and method thereof can be used for studying gene expression, for example, using an antisense nucleic acid.

In the discussion starting on page 58, the Applicants describe the use of the expression construct to study the expression of reporter genes in cells. Data are also presented of the results of such a study.

In the discussion starting on page 69, the Applicants have described that the expression constructs can be used to study the effects of certain gene products as potential therapeutics in, for example, animal models of disease.

In light of the above, Applicants request the withdrawal of the rejection under 35 U.S.C. § 112, first paragraph ("enablement").

Concerning the rejection under 35 U.S.C. § 112, first paragraph, ("written description"), the present claims define that the HIV-2 promoter sequence is operably linked to a selected polynucleotide and an inducible promoter sequence is operably linked to a transactivating factor, which binds to and activates the HIV-2 promoter. The components of the expression vector are specifically aligned in terms of the 5' to 3' orientation. The inducible promoter is described on pages 14-16 and 33-34. The transactivating factor, which

binds to and activates the HIV-2 promoter is known and the HIV protein tat is described as an example. The tat transactivator is provided in Claim 49. In addition, at the time of filing this application it was recognized in the art that there were other proteins which could transactivate the HIV-promoter. Dasgupta et al[1] describe that the cellular myb transcription factor binds to and transactivates HIV promoters. Arya and Sethi[2] describe that HIV promoter transactivation by the IE-2 protein of cytomegalovirus. Kashanchi et al[3] describe tranactivation of HIV promoters with an ORF-1 protein from human herpesvirus. Bassuk et al[4] describe transactivation of HIV promoters mediated by Ets and NF-κB/NFAT proteins. Lastly, Pereira et al[5] summarizes a multitude of cellular transcription proteins that bind to and activate the HIV promoters. Although Pereira et al was published after this application was filed, many of the references that support the summary were, in fact, known at the time the present application was filed.

Therefore, Applicants request the withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, (written description).

THE REJECTIONS UNDER 35 U.S.C. §§ 102 AND 103

The present claims are directed to an expression construct with an HIV-2 promoter sequence operably linked to a selected polynucleotide and an inducible promoter sequence operably linked to a HIV promoter transactivating factor. The relative 5' to 3' orientation of the components is also specified. Such an expression construct is not described in any of the references cited and therefore, the rejections over the prior art are untenable in light of the claims submitted herein.

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[1] *Proc. Natl. Acad. Sci. USA* 87:8090-8094 (1990).
[2] *AIDS Research and Human Retroviruses* 6(5):649-658 (1990).
[3] *Virology* 201:95-106 (1994).
[4] *Journal of Virology* 71(5):3563-3573 (1997).
[5] *Nucleic Acids Research* 28(3): 663-668 (2000).

Furthermore, the cited prior art does not describe the advantage of utilizing an HIV-2 promoter compared to an HIV-1 promoter or the relative orientation as in the present claims. The importance of these features of the expression construct is of record and also discussed in the declaration of Dr. Harris, which was previously provided to the Office.

In addition, Applicants direct the Examiner's attention to Table 4 on page 66 in which the results of testing various constructs to induce the expression of IL-2 are presented. In particular, Applicants refer the Examiner to the vectors F12 and 007:

(1) the F12 vector contains the HIV-1 promoter driving expression of IL-2 upstream of the HSP promoter driving the expression of the tat gene (for reference see Figure 9C);

(2) the 007 vector utilizes the HIV-2 promoter driving the expression of IL-2 upstream of the HSP promoter driving the expression of the tat gene (see Figure 9D).

For reference, Table 4 is reproduced below:

TABLE 4

	I.U. of IL-2				
temperature	37°C	39°C	41°C	42 °C	44°C
heat shock duration:	continuous	continuous	1 hr	1 hr	0.5 hr
Lipid alone	2.03	0.50	0.41	0.53	0.53
L-27	14.28	9.88	5.95	9.88	7.80
007	336.76	318.49	334.02	373.74	389.27
F12	78.40	106.88	149.93	230.02	188.13
C8	9.19	8.03	11.74	8.73	16.37

As shown in Table 4, the 007 vector demonstrated significantly higher IL-2 expression relative to the F12 vector. In addition, the 007 vector demonstrated significantly higher IL-2 expression levels than the L27 vector which utilizes the CMV promoter. As discussed by Dr. Harris in his Declaration, these data were neither described or could have been expected from the disclosures provided in the prior art, in particular, Bromley et al.

Bromley et al describe one construct containing the HIV-tat transactivator under the control of a heat-shock promoter. The tat, in turn, transactivates a gene of interest under the control of an HIV-LTR, which is found on a second construct. As the core basis of the rejections of record, Bromley et al suggest that the two expression constructs can be put on the same construct. No further discussion for constructing dual gene expression constructs is provided in Bromley et al. In particular, Bromley et al do not describe selecting an HIV-2 promoter rather than an HIV-1 promoter or to position the promoters and polynucleotides in the relative 5' to 3' orientation as in the present claims.

Likewise, the remaining references when combined with Bromley et al also fail to describe these features of the present claims as well as the attendant advantages therein as supported by the data provided in the specification and the discussion provided by Dr. Harris.

Therefore, Bromley et al combined with one or more of Gage et al (U.S. Patent No. 5,770,414), Stover (U.S. Patent No. 5,583,038), Hickey et al, Gaestel et al, Dale, Quail et al (EP 0342926), Dubensky (U.S. Patent No. 5,814,482), Scott et al (WO 95/09913), Saito et al (U.S. Patent No. 5,817,492), Weinberg et al (WO 89/10412), Beach et al (U.S. Patent No. 5,889,169), Tewari et al, Emerman et al, Loeb et al (U.S. Patent No. 5,877,010), Hancock, and Talavera fail to provide the requisite description to support a *prima facie* case of obviousness. Even if there was some modicum of suggestion, the combination of prior art

fails to provide any suggestion for the advantages that the claimed expression construct provides.

In light of the above, Applicants request that the rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The rejection concerning Claims 20-22 under 35 U.S.C. § 112, second paragraph, is obviated by the cancellation of these claims.

In the event the Examiner has any questions or wishes to discuss any issue in this application, he is invited to contact the Applicants' undersigned representative to resolve the matter expediently.

Applicants respectfully request that this application be passed onto issuance.

Respectfully submitted,

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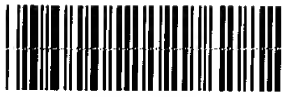

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IN THE CLAIMS

Claims 1, 5, 9-18, 20-26, 33, 35-39 and 43-47 (Cancelled).

Claims 48-75 (New).